3/13/05 10/765,227 c.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 21:51:37 ON 13 MAR 2005 Structure search (c)

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 21:51:45 ON 13 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 MAR 2005 HIGHEST RN 845457-93-4
DICTIONARY FILE UPDATES: 11 MAR 2005 HIGHEST RN 845457-93-4

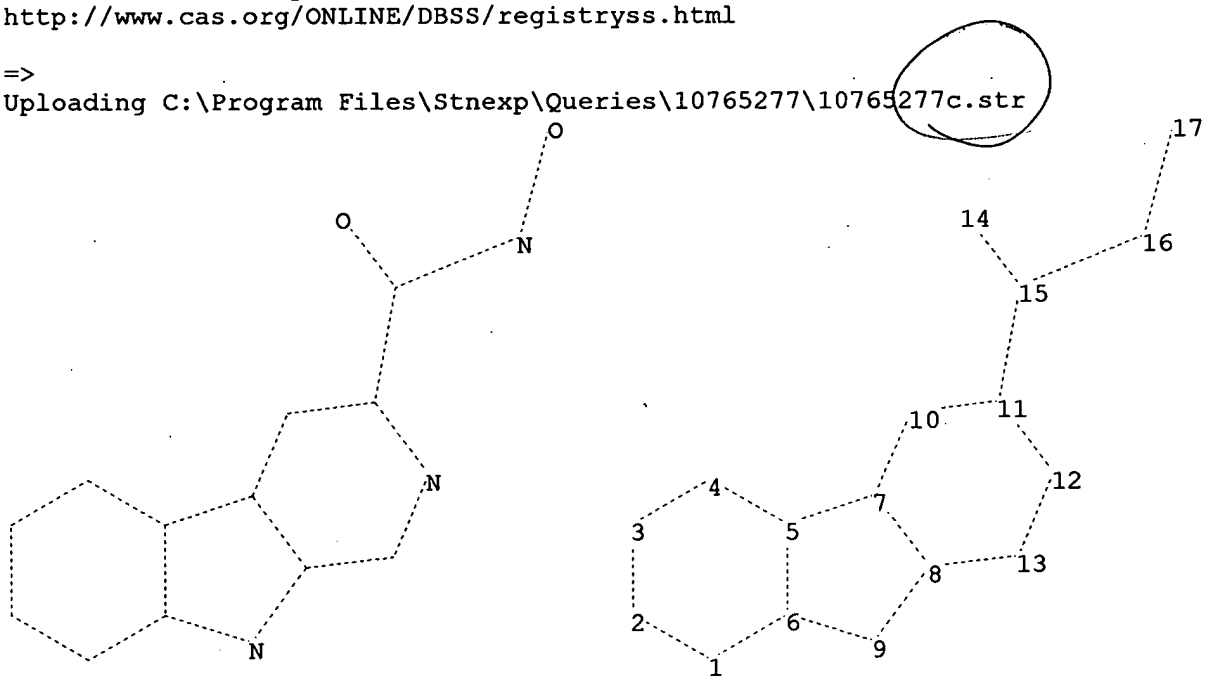
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10765277\10765277c.str



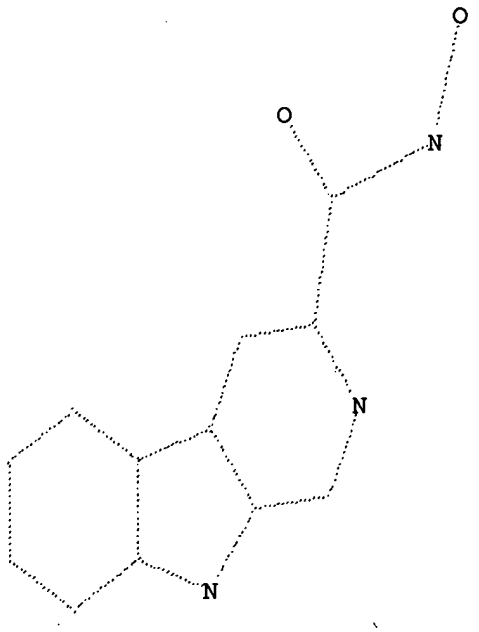
chain nodes :

14 15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
chain bonds :
11-15 14-15 15-16 16-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 12-13
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 11-15
12-13 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L1   STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 21:52:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   29 TO ITERATE

100.0% PROCESSED   29 ITERATIONS   3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 257 TO   903
PROJECTED ANSWERS: 3 TO   163

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L2             3 SEA SSS SAM L1

=> s L1 full
FULL SEARCH INITIATED 21:52:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    665 TO ITERATE

100.0% PROCESSED     665 ITERATIONS                          61 ANSWERS
SEARCH TIME: 00.00.01

L3            61 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY     SESSION
FULL ESTIMATED COST                          161.33      161.54

FILE 'CAPLUS' ENTERED AT 21:52:18 ON 13 MAR 2005
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FILE COVERS 1907 - 13 Mar 2005  VOL 142 ISS 12
FILE LAST UPDATED: 11 Mar 2005  (20050311/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s L3
L4             12 L3

=> d ibib abs hitstr 1-12

L4   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:648524  CAPLUS
DOCUMENT NUMBER:          141:207055
TITLE:                    Preparation of β-carboline hydroxamic acids as
                          HIV-integrase inhibitors
INVENTOR(S):              Kuki, Atsuo; Li, Xinqiang; Plewe, Michael Bruno; Wang,
                          Hai; Zhang, Junhu
PATENT ASSIGNEE(S):       Pfizer Inc., USA
SOURCE:                   PCT Int. Appl., 57 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ----------------     ----   --------    --------------------     --------
     WO 2004067531         A1    20040812    WO 2004-IB259            20040123
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W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRIORITY APPLN. INFO.: US 2003-443223P P 20030127

OTHER SOURCE(S): MARPAT 141:207055

GI

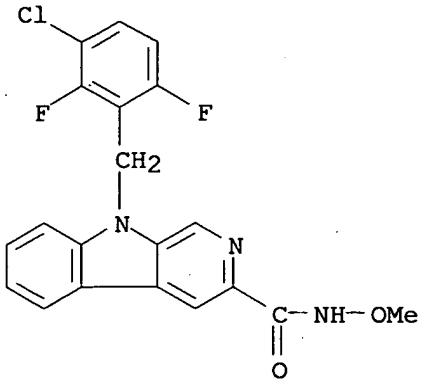
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Beta-carboline hydroxamic acid compds. Title compds. I and II [wherein R1, R2, R3, R4, R5, R6 = independently H, halo, alkoxy/alkyl, alkenyl, alkynyl, OH and derivs., NO2, NH2 and derivs.; R7 = (un)substituted alk(en/yn)yl; R8, R9 = independently H, (un)substituted alk(en/yn)yl; X = (CR10R11)n; R10, R11 = independently H, halo, OH and derivs., NH and derivs., (un)substituted lower alk(en/yn)yl; n = 1-3; their pharmaceutically acceptable salts and solvates] were prepared as inhibitors or modulators the activity of HIV-integrase enzyme. Examples include 13 synthetic prepns., bioassays for HIV-integrase activity and HIV-1 cell protection. For example, III was prepared, in 39% yield, from Et 9H-3-carboline-3-carboxylate, 4-fluorobenzyl bromide and NH2OH. Selected I and II displayed IC50 values in the range of 0.234 - 0.713 μM for the inhibition of HIV-integrase. Thus, I and II are useful for treating HIV-integrase-mediated diseases and conditions (no data).

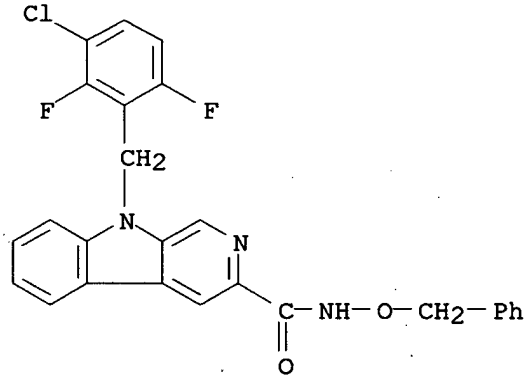
IT **737817-45-7P 737817-46-8P 737817-47-9P,** 9-(4-Fluorobenzyl)-N-hydroxy-9H-β-carboline-3-carboxamide **737817-48-0P,** 9-[(5-Chlorothien-2-yl)methyl]-N-hydroxy-9H-β-carboline-3-carboxamide **737817-49-1P,** 9-(3-Chloro-2-fluorobenzyl)-N-hydroxy-9H-β-carboline-3-carboxamide **737817-50-4P,** 9-Benzyl-N-hydroxy-9H-β-carboline-3-carboxamide **737817-51-5P,** 9-(4-Methylbenzyl)-N-Hydroxy-9H-β-carboline-3-carboxamide **737817-52-6P,** 9-(2,4-Difluorobenzyl)-N-hydroxy-9H-3-carboline-3-carboxamide **737817-53-7P,** 9-(3-Chloro-2,6-difluorobenzyl)-N-hydroxy-9H-β-carboline-3-carboxamide **737817-56-0P,** 6-Amino-9-(3-chlorobenzyl)-N-hydroxy-9H-β-carboline-3-carboxamide **737817-59-3P,** 9-(3-Chloro-2,6-difluorobenzyl)-N-hydroxy-N-methyl-9H-β-carboline-3-carboxamide **737817-60-6P,** N-Benzyl-9-(3-chloro-2,6-difluorobenzyl)-N-hydroxy-9H-β-carboline-3-carboxamide **737817-61-7P,** 9-(4-Fluorobenzyl)-N-hydroxy-N-methyl-9H-β-carboline-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HIV-inhibitor; preparation of β-carboline hydroxamic acids as HIV-integrase inhibitors)

RN 737817-45-7 CAPLUS

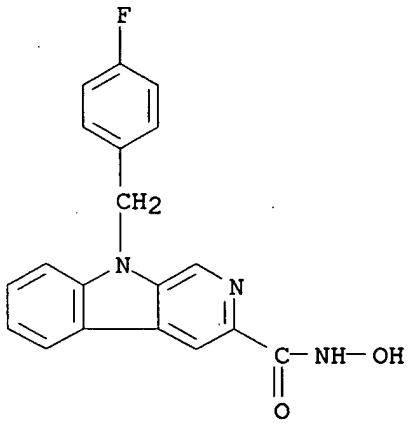
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2,6-difluorophenyl)methyl]-N-methoxy- (9CI) (CA INDEX NAME)



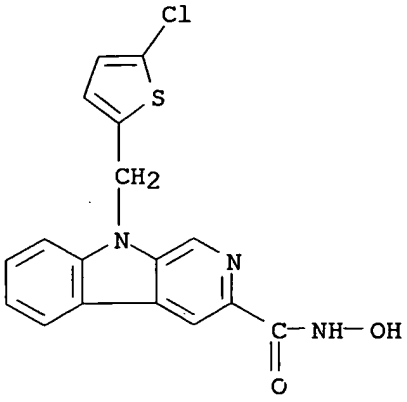
RN 737817-46-8 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2,6-difluorophenyl)methyl]-N-(phenylmethoxy)- (9CI) (CA INDEX NAME)



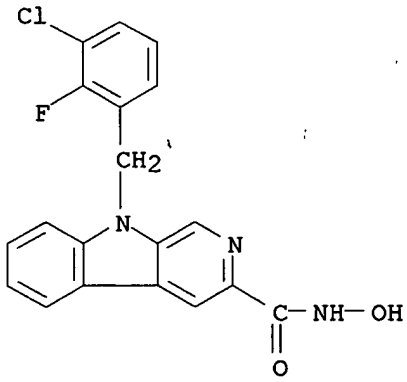
RN 737817-47-9 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(4-fluorophenyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



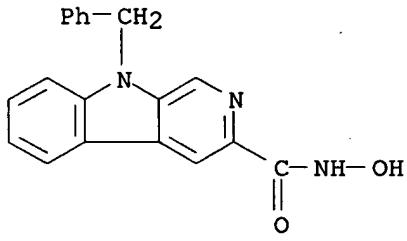
RN 737817-48-0 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(5-chloro-2-thienyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



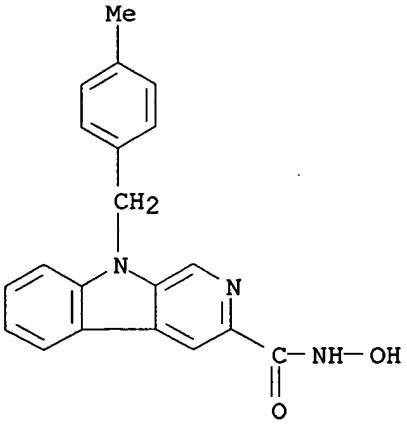
RN 737817-49-1 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2-fluorophenyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



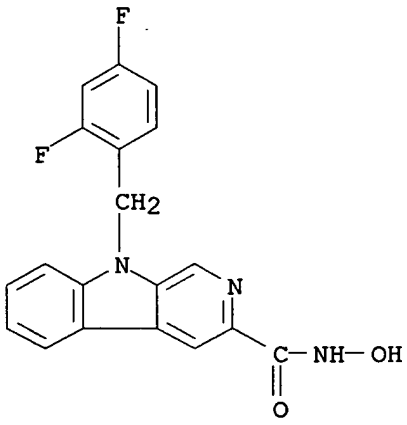
RN 737817-50-4 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, N-hydroxy-9-(phenylmethyl)- (9CI) (CA INDEX NAME)



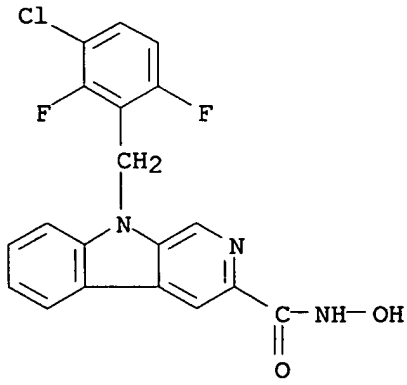
RN 737817-51-5 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, N-hydroxy-9-[(4-methylphenyl)methyl]-(9CI) (CA INDEX NAME)



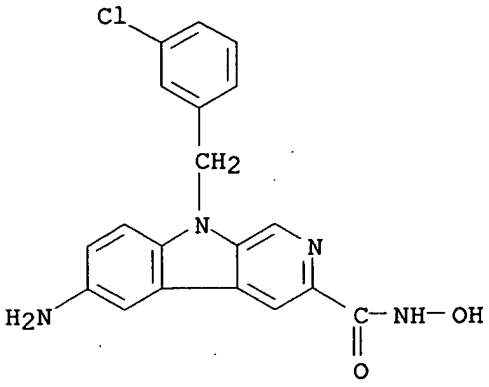
RN 737817-52-6 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(2,4-difluorophenyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



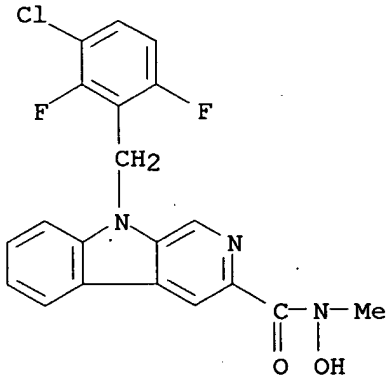
RN 737817-53-7 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2,6-difluorophenyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



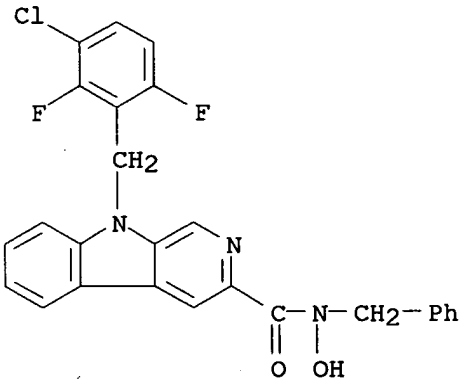
RN 737817-56-0 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 6-amino-9-[(3-chlorophenyl)methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



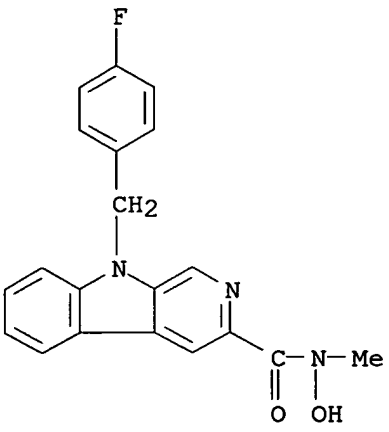
RN 737817-59-3 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2,6-difluorophenyl)methyl]-N-hydroxy-N-methyl- (9CI) (CA INDEX NAME)



RN 737817-60-6 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(3-chloro-2,6-difluorophenyl)methyl]-N-hydroxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 737817-61-7 CAPLUS
CN 9H-Pyrido[3,4-b]indole-3-carboxamide, 9-[(4-fluorophenyl)methyl]-N-hydroxy-N-methyl- (9CI) (CA INDEX NAME)

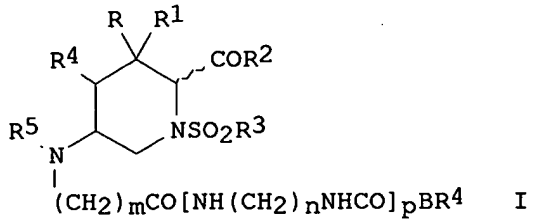


L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:695985 CAPLUS
DOCUMENT NUMBER: 137:216938
TITLE: Preparation of polycyclic piperidine derivatives as metalloproteinase inhibitors
INVENTOR(S): De Nanteuil, Guillaume; Benoist, Alain; Lefoulon, Francois; Hickman, John; Pierre, Alain; Tucker, Gordon; Bridon, Dominique; Ezrin, Alan; Holmes, Darren; Huang, Xicai
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Conjuchem Inc.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070521	A1	20020912	WO 2002-FR800	20020306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
FR 2821842	A1	20020913	FR 2001-3068	20010307
FR 2821842	B1	20030509		

PRIORITY APPLN. INFO.: FR 2001-3068 A 20010307
OTHER SOURCE(S): MARPAT 137:216938
GI



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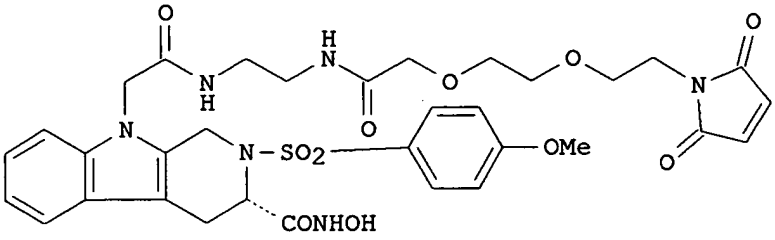


II

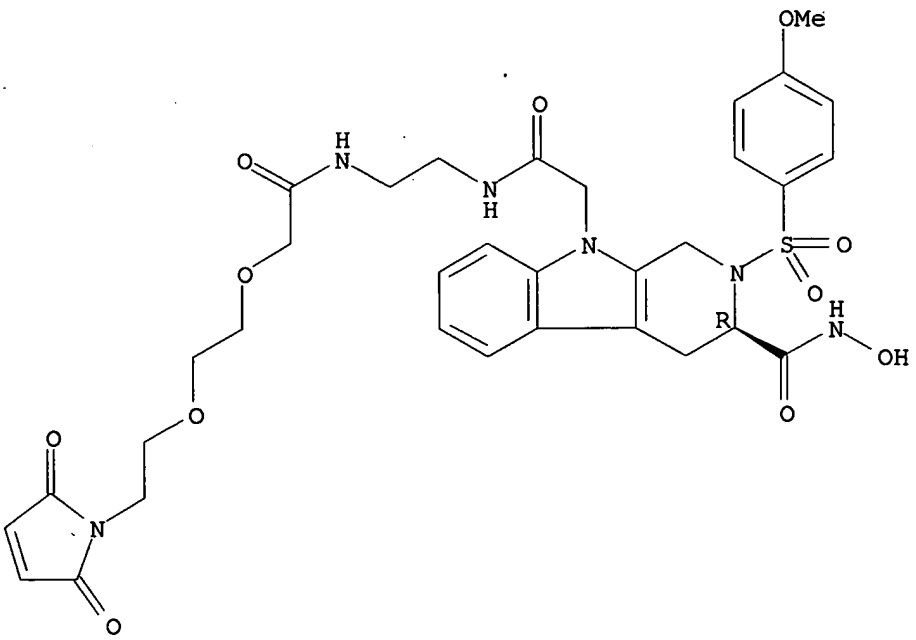
AB Title compds. I [R, R1 = H, alkyl; R2 = H, OH, NHOH; R3 = (un)substituted Ph, 4-PhC6H4; R4 = group capable of forming a covalent bond with mobile proteins of the blood; R5R6 = atoms required to complete a mono- or bicyclic nitrogen heterocycle; B = bond, alkylene, oxaalkylene thiaalkylene, azaalkylene; m = 0-6; n = 1-6; p = 0, 1] their isomers and their addition salts with a pharmaceutically acceptable acid or a base, were prepared for use as metalloproteinase inhibitors in the treatment of cancer. Thus, the β-carboline II, prepared in a multi-step synthesis, had IC50 87nM for inhibition of MMP-2.

IT **455884-29-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polycyclic piperidine derivs. as metalloproteinase inhibitors)

RN 455884-29-4 CAPLUS

CN 9H-Pyrido[3,4-b]indole-9-acetamide, N-[2-[[[2-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethoxy]ethoxy]acetyl]amino]ethyl]-1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

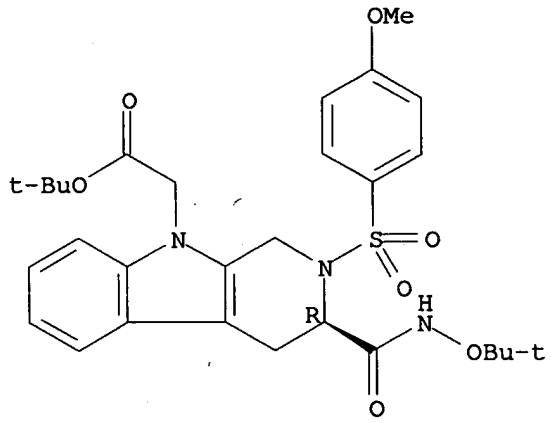


IT **455884-24-9P 455884-26-1P 455884-27-2P**
455884-28-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polycyclic piperidine derivs. as metalloproteinase inhibitors)

RN 455884-24-9 CAPLUS

CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 3-[[(1,1-dimethylethoxy)amino]carbonyl]-1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-, 1,1-dimethylethyl ester, (3R)- (9CI) (CA INDEX NAME)

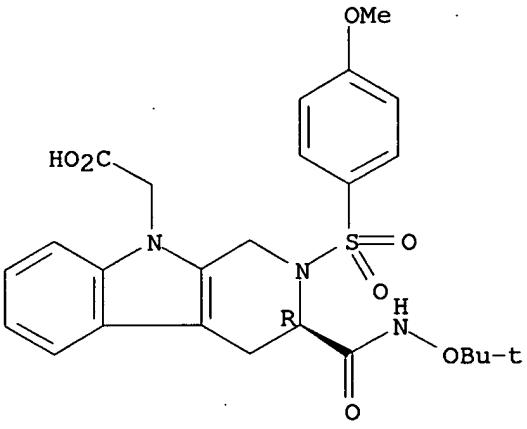
Absolute stereochemistry.



RN 455884-26-1 CAPLUS

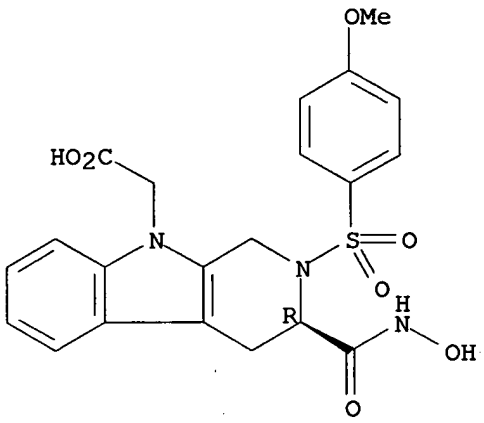
CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 3-[[(1,1-dimethylethoxy)amino]carbonyl]-1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



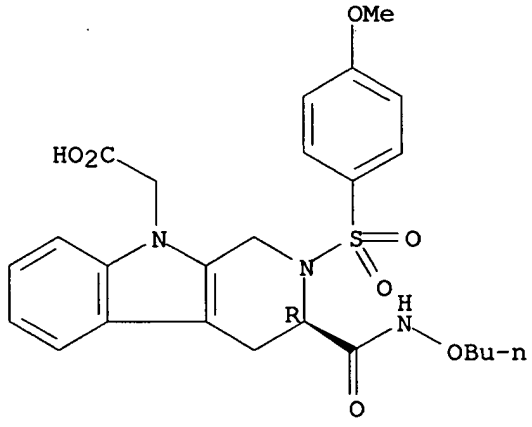
RN 455884-27-2 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



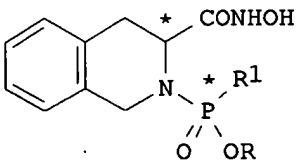
RN 455884-28-3 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 3-[(butoxyamino)carbonyl]-1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:35359 CAPLUS
DOCUMENT NUMBER: 136:263211
TITLE: New Type of Metalloproteinase Inhibitor: Design and Synthesis of New Phosphonamide-Based Hydroxamic Acids
AUTHOR(S): Sawa, Masaaki; Kiyoi, Takao; Kurokawa, Kiriko; Kumihara, Hiroshi; Yamamoto, Minoru; Miyasaka, Tomohiro; Ito, Yasuko; Hirayama, Ryoichi; Inoue, Tomomi; Kirii, Yasuyuki; Nishiwaki, Eiji; Ohmoto, Hiroshi; Maeda, Yu; Ishibushi, Etsuko; Inoue, Yoshimasa; Yoshino, Kohichiro; Kondo, Hirosato
CORPORATE SOURCE: Department of Chemistry, R&D Laboratories, Nippon Organon, K.K., Miyakojima-ku, Osaka, 534-0016, Japan
SOURCE: Journal of Medicinal Chemistry (2002), 45(4), 919-929
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:263211
GI



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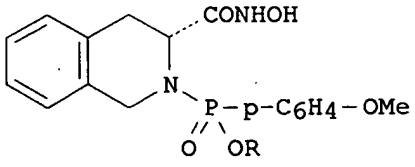
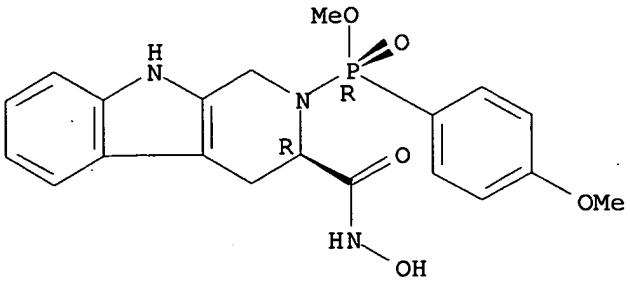


II

AB Some phosphonamide-based hydroxamate derivs., mainly I (R = alkyl, substituted alkyl, R1 = aryl, arylalkyl; * marks chiral centers at C-3 and P), were synthesized, and their inhibitory activities were evaluated against various metalloproteinases to clarify their selectivity profile. Among the four diastereomeric isomers resulting from the chirality at the C-3 and P atoms, the compound with a (R,R)-configuration both at the C-3 position and the P atom was potently active, while the other diastereomeric isomers were almost inactive. A number of (R,R)-compds. synthesized here, e.g., II (R = Me, Et, Bu, hexyl, Pr-i, CH2C6H11, (CH2)2Ph, (CH2)2C6H4Ph-p, (CH2)2NEt2, 2-(2-pyridinyl)ethyl, (CH2)2OEt), exhibited broad spectrum activities with nanomolar Ki values against MMP-1, -3, -9, and TACE and also showed nanomolar IC50 values against HB-EGF shedding in a cell-based inhibition assay. The modeling study using x-ray structure of MMP-3 suggested the possible binding mode of the phosphonamide-based inhibitors.

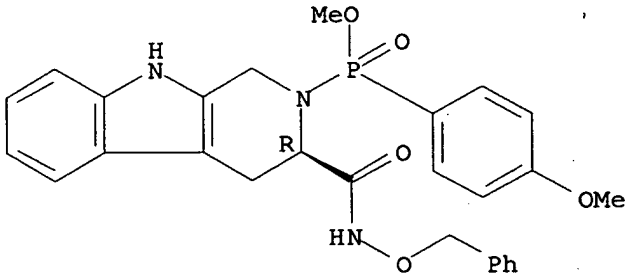
IT **362474-98-4P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(HPLC separation; design and synthesis of phosphonamide-based hydroxamic acids as new types of metalloproteinase inhibitors)
RN 362474-98-4 CAPLUS
CN Phosphinic acid, (4-methoxyphenyl)[(3R)-1,3,4,9-tetrahydro-3-[(hydroxyamino)carbonyl]-2H-pyrido[3,4-b]indol-2-yl]-, methyl ester, [P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



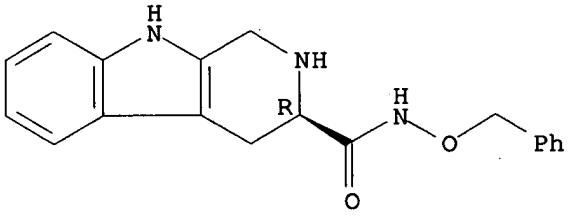
IT **362476-89-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)
RN 362476-89-9 CAPLUS
CN Phosphinic acid, (4-methoxyphenyl)[(3R)-1,3,4,9-tetrahydro-3-[[(phenylmethoxy)amino]carbonyl]-2H-pyrido[3,4-b]indol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **362477-35-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with phosphonyl monochloride)
RN 362477-35-8 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-(phenylmethoxy)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:713177 CAPLUS
DOCUMENT NUMBER: 135:251992
TITLE: Keratinocyte growth inhibitors and hydroxamic acid derivatives

INVENTOR(S): Hashimoto, Koji; Higashiyama, Shigeki; Yoshino, Kohichiro; Yoshiizumi, Kazuya; Yamamoto, Minoru; Kiyoi, Takao; Kurokawa, Kiriko; Kondo, Hirosato; Sawa, Masaaki; Kumihara, Hiroshi

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

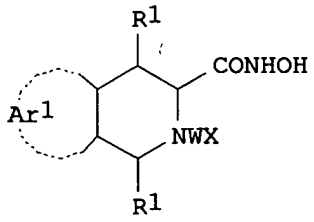
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070269	A1	20010927	WO 2001-JP2251	20010322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001039549	A5	20011003	AU 2001-39549	20010322
US 2003229113	A1	20031211	US 2003-239675	20030219
PRIORITY APPLN. INFO.:			JP 2000-84126 A	20000324
			JP 2000-120430 A	20000421
			JP 2000-394983 A	20001226
			WO 2001-JP2251 W	20010322

OTHER SOURCE(S): MARPAT 135:251992

GI



I

AB Disclosed are keratinocyte growth inhibitors containing as the active ingredient compds. inhibiting an enzyme solubilizing a heparin-binding epidermal growth factor-like growth factor (HB-EGF); and novel hydroxamic acid derivs. represented by the following general formula I which have an effect of inhibiting an enzyme solubilizing a heparin-binding epidermal growth factor-like growth factor, wherein Ar1 = aromatic 6-membered ring, etc.; R1 = H or Me; W = SO2- or P(O)(OR)-; and X = substituted benzene ring, etc. A compound (+)-N-hydroxy-6-(4-methoxybenzenesulfonyl)-5,6,7,8-tetrahydropyrido[3,4-b]pyrazine-7-carboxamide (II) was prepared, and examined for its inhibitory effect on TPA-induced keratinocyte growth in mice. Also, a tablet containing II 100, corn starch 46, crystalline cellulose 98, hydroxypropyl cellulose 2, and magnesium stearate 4 mg was formulated.

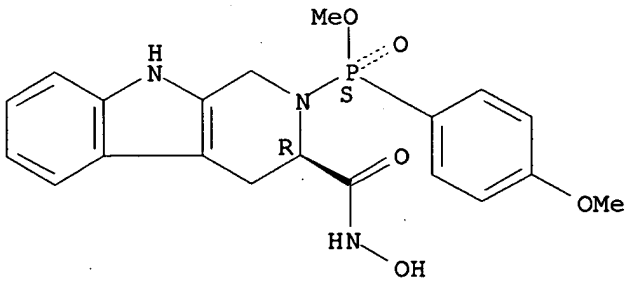
IT **362474-97-3P 362474-98-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acid derivs. as keratinocyte growth inhibitors)

RN 362474-97-3 CAPLUS

CN Phosphinic acid, (4-methoxyphenyl)[(3R)-1,3,4,9-tetrahydro-3-[(hydroxyamino)carbonyl]-2H-pyrido[3,4-b]indol-2-yl]-, methyl ester, [P(S)]- (9CI) (CA INDEX NAME)

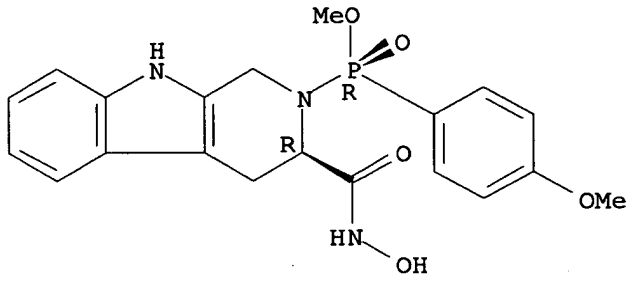
Absolute stereochemistry.



RN 362474-98-4 CAPLUS

CN Phosphinic acid, (4-methoxyphenyl)[(3R)-1,3,4,9-tetrahydro-3-[(hydroxyamino)carbonyl]-2H-pyrido[3,4-b]indol-2-yl]-, methyl ester, [P(R)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **362476-89-9P 362477-35-8P 362477-36-9P**

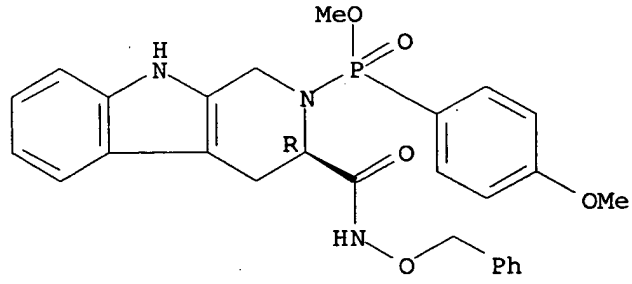
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxamic acid derivs. as keratinocyte growth inhibitors)

RN 362476-89-9 CAPLUS

CN Phosphinic acid, (4-methoxyphenyl)[(3R)-1,3,4,9-tetrahydro-3-[[(phenylmethoxy)amino]carbonyl]-2H-pyrido[3,4-b]indol-2-yl]-, methyl ester (9CI) (CA INDEX NAME)

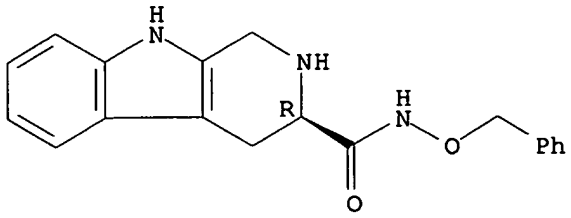
Absolute stereochemistry.



RN 362477-35-8 CAPLUS

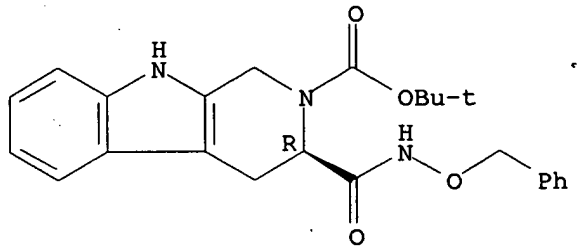
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-(phenylmethoxy)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 362477-36-9 CAPLUS
CN 2H-Pyrido[3,4-b]indole-2-carboxylic acid, 1,3,4,9-tetrahydro-3-[[(phenylmethoxy)amino]carbonyl]-, 1,1-dimethylethyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

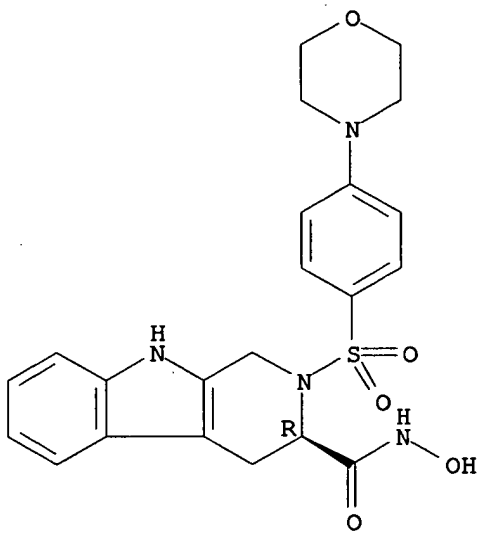
L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:652921 CAPLUS
DOCUMENT NUMBER: 132:18475
TITLE: Affinity and Selectivity of Matrix Metalloproteinase Inhibitors: A Chemometrical Study from the Perspective of Ligands and Proteins
AUTHOR(S): Matter, Hans; Schwab, Wilfried
CORPORATE SOURCE: Hoechst Marion Roussel Chemical Research, Frankfurt am Main, D-65926, Germany
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4506-4523
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel strategy to understand affinity and selectivity for enzyme inhibitors using information from ligands and target protein 3D structures is described. It was applied to 2-arylsulfonyl-1,2,3,4-tetrahydro-isoquinoline-3-carboxylates and -hydroxamates as inhibitors of the matrix metalloproteinases MMP-3 (stromelysin-1) and MMP-8 (human neutrophil collagenase). As the first step, consistent and predictive 3D-QSAR models were derived using CoMFA, CoMSIA, and GRID/Golpe approaches, leading to the identification of binding regions where steric, electronic, or hydrophobic effects are important for affinity. These models were validated using multiple analyses using two or five randomly chosen cross-validation groups and randomizations of biol. activities. Second, 3D-QSAR models were derived based on the affinity ratio

IC50(MMP-8)/IC50(MMP-3), allowing the identification of key ligand determinants for selectivity toward one of both enzymes. In addition to this ligands' view, the third step encompasses a chemometrical approach based on principal component anal. (PCA) of multivariate GRID descriptors to uncover the major differences between both protein binding sites with respect to their GRID probe interaction pattern. The resulting information, based on the accurate knowledge of the target protein 3D structures, led to a consistent picture in good agreement with exptl. observed differences in selectivity toward MMP-8 or MMP-3. The interpretation of all three classes of statistical models leads to detailed SAR information for MMP inhibitors, which is in agreement with available data for binding site topologies, ligand affinities, and selectivities. Thus the combined chemical analyses provide guidelines and accurate activity predictions for designing novel, selective MMP inhibitors.

IT **191326-74-6 191326-90-6 191326-91-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(affinity and selectivity of matrix metalloproteinase inhibitors: chemometrical study from perspective of ligands and proteins)

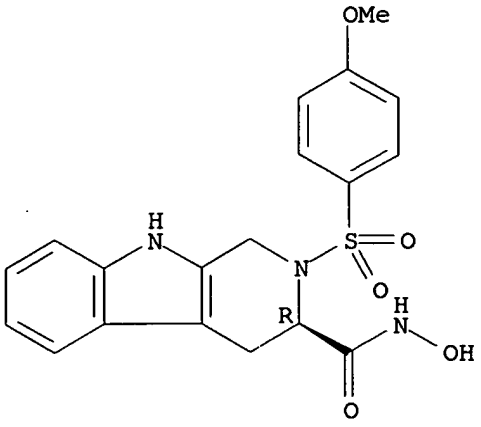
RN 191326-74-6 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[[4-(4-morpholinyl)phenyl]sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



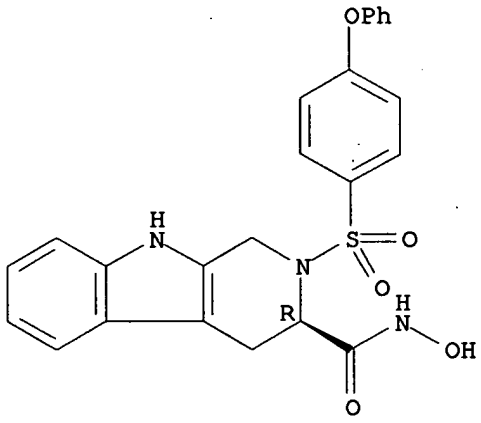
RN 191326-90-6 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 191326-91-7 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-phenoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:465692 CAPLUS
DOCUMENT NUMBER: 131:87907
TITLE: Preparation of carbolinecarboxamide derivatives as metalloprotease inhibitors
INVENTOR(S): De Nanteuil, Guillaume; Remond, Georges; Paladino, Joseph; Atassi, Ghanem; Pierre, Alain; Tucker, Gordon; Bonnet, Jacqueline; Sabatini, Massimo
PATENT ASSIGNEE(S): Adir et Cie., Fr.
SOURCE: Fr. Demande, 26 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

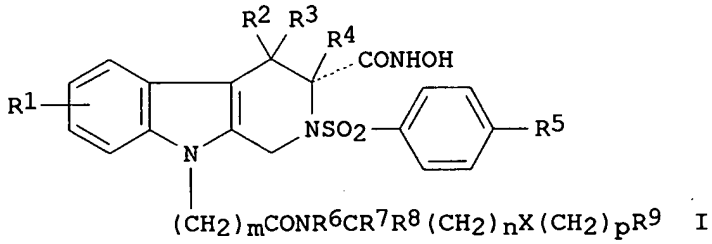
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2771095	A1	19990521	FR 1997-14278	19971114

FR 2771095	B1	19991217			
NO 9805239	A	19990518	NO 1998-5239		19981110
NO 311723	B1	20020114			
CA 2254152	C	20030408	CA 1998-2254152		19981112
CA 2254152	AA	19990514			
EP 916671	A1	19990519	EP 1998-402806		19981113
EP 916671	B1	20020130			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
ZA 9810411	A	19990524	ZA 1998-10411		19981113
CN 1217332	A	19990526	CN 1998-122312		19981113
AU 9892377	A1	19990603	AU 1998-92377		19981113
AU 740313	B2	20011101			
JP 11209378	A2	19990803	JP 1998-323208		19981113
US 6066633	A	20000523	US 1998-191323		19981113
BR 9805014	A	20010424	BR 1998-5014		19981113
AT 212634	E	20020215	AT 1998-402806		19981113
PT 916671	T	20020628	PT 1998-402806		19981113
ES 2172101	T3	20020916	ES 1998-402806		19981113

PRIORITY APPLN. INFO.: FR 1997-14278 A 19971114

OTHER SOURCE(S): MARPAT 131:87907

GI



I

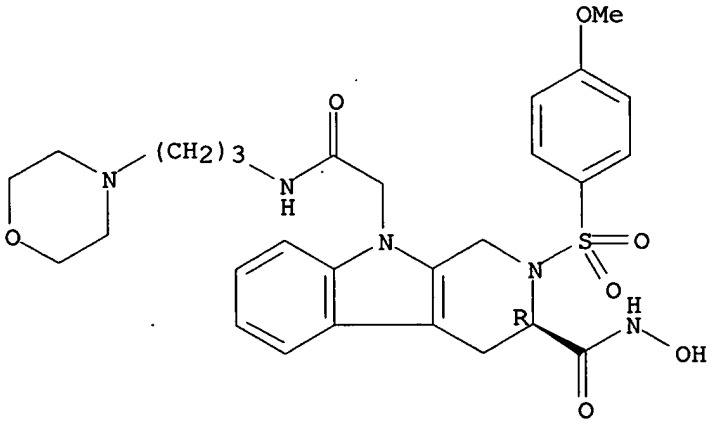
AB The title compds. I [m = 1-4; n, p = 0-4; X = O, S, bond; R1 = H, halo, alkyl, OH, etc.; R2, R3, R4 = H, alkyl; R6, R7, R8 = H, alkyl or form a heterocycle; R5 = H, halo, alkoxy, aryloxy, heteraryloxy; R9 = SO3H, ester group, etc.], metalloprotease inhibitors, were prepared E.g., 2-(4-methoxybenzenesulfonyl)-9-[(3-morpholin-4-ylpropylcarbamoyl)methyl]-2,3,4,9-tetrahydro-1H-β-carboline-(3R)-N-hydroxycarboxamide hydrochloride was prepared

IT **229974-68-9P 229974-70-3P 229974-71-4P**
229974-72-5P 229974-73-6P 229974-74-7P
229974-75-8P 229974-76-9P 229974-77-0P
229974-78-1P 229974-79-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carbolinecarboxamide derivs. as metalloprotease inhibitors)

RN 229974-68-9 CAPLUS

CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[3-(4-morpholinyl)propyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



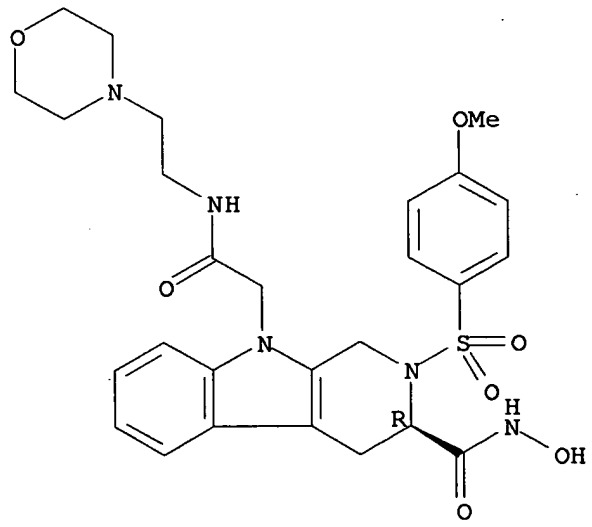
● HCl

RN 229974-70-3 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[2-(4-morpholinyl)ethyl]-, (3R)-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

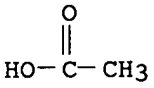
CRN 229974-69-0
CMF C27 H33 N5 O7 S

Absolute stereochemistry.



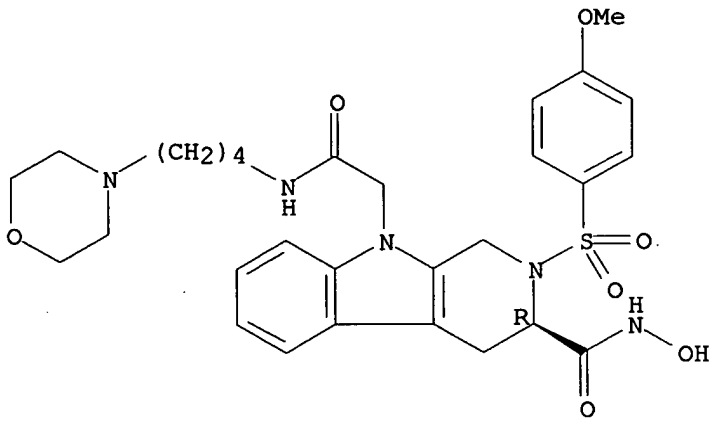
CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 229974-71-4 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[4-(4-morpholinyl)butyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

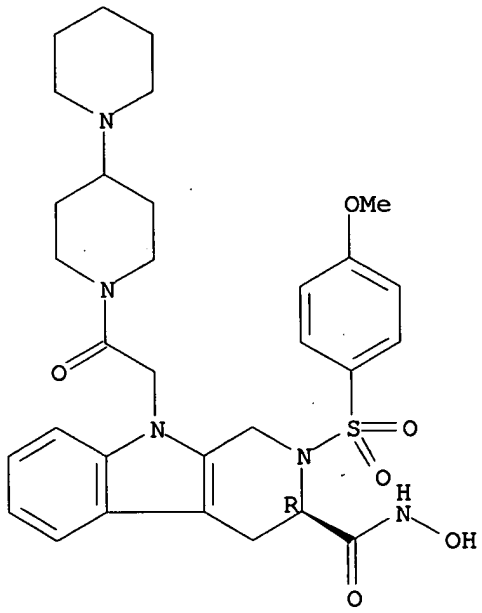
Absolute stereochemistry.



● HCl

RN 229974-72-5 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 9-(2-[1,4'-bipiperidin]-1'-yl-2-oxoethyl)-2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

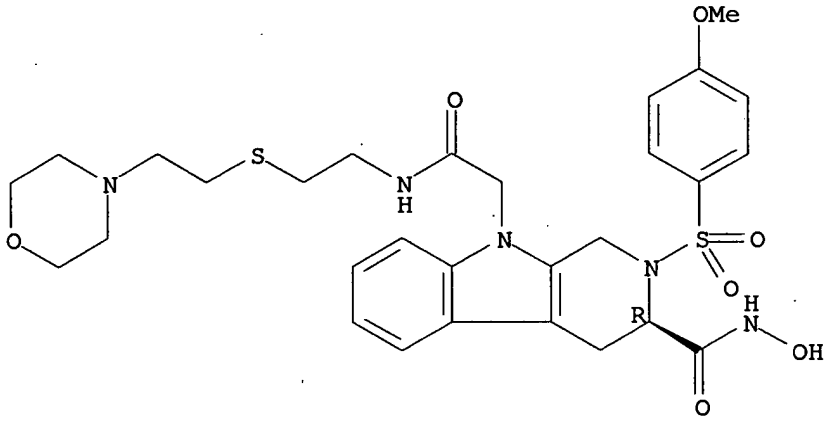
Absolute stereochemistry.



● HCl

RN 229974-73-6 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[2-[[2-(4-morpholinyl)ethyl]thio]ethyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

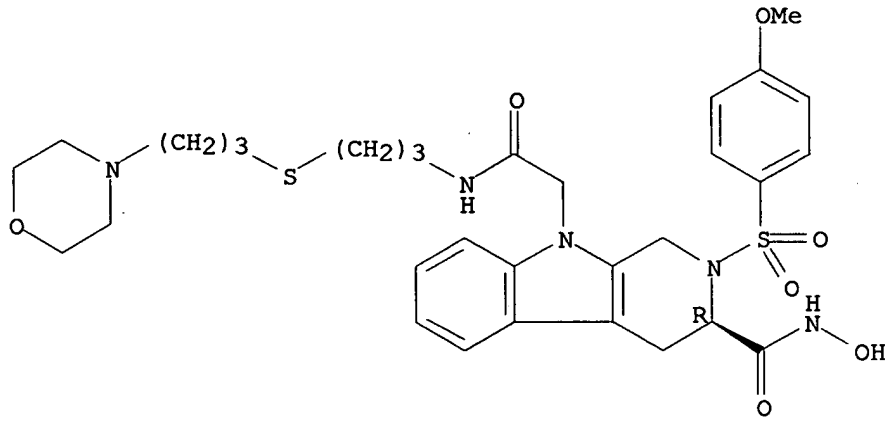
Absolute stereochemistry.



● HCl

RN 229974-74-7 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[3-[[3-(4-morpholinyl)propyl]thio]propyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

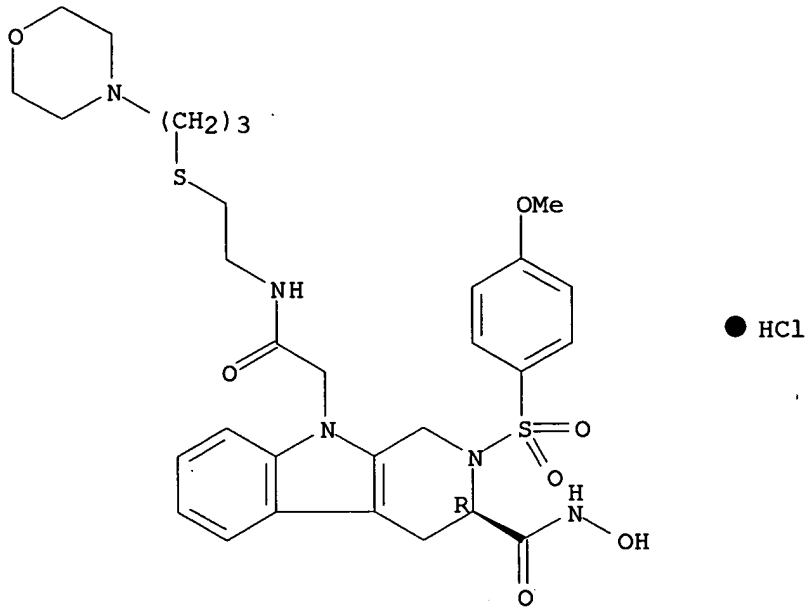


● HCl

RN 229974-75-8 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[2-[[3-(4-morpholinyl)propyl]thio]ethyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX

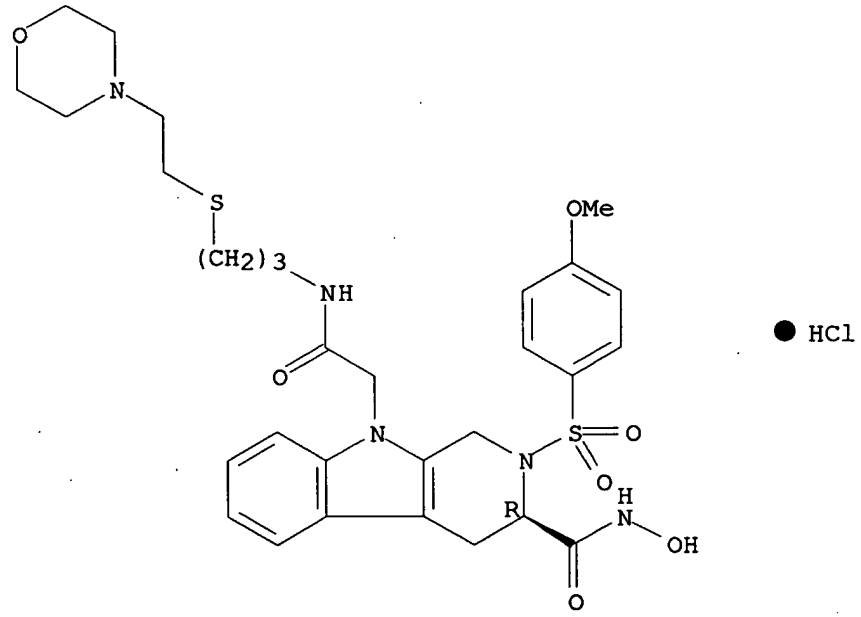
NAME)

Absolute stereochemistry.



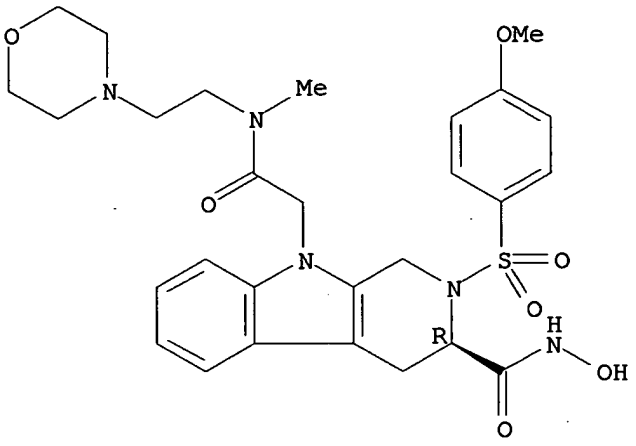
RN 229974-76-9 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-[3-[[2-(4-morpholinyl)ethyl]thio]propyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 229974-77-0 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-N-methyl-N-[2-(4-morpholinyl)ethyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

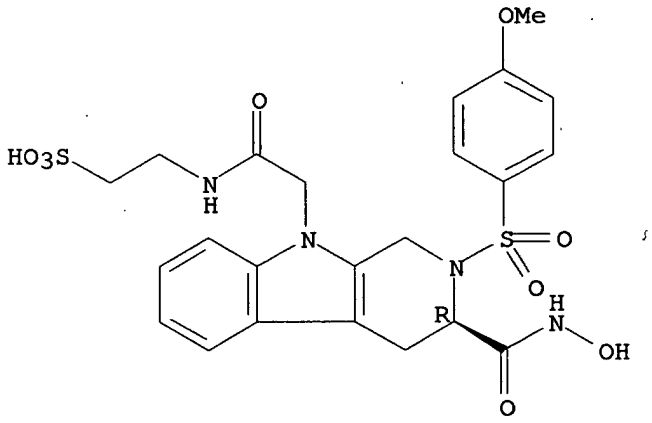
Absolute stereochemistry.



● HCl

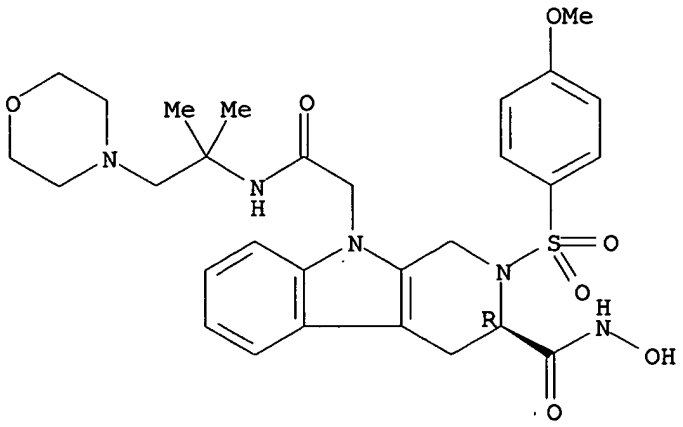
RN 229974-78-1 CAPLUS
CN Ethanesulfonic acid, 2-[[[(3R)-1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-9H-pyrido[3,4-b]indol-9-yl]acetyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 229974-79-2 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, N-[1,1-dimethyl-2-(4-morpholinyl)ethyl]-1,2,3,4-tetrahydro-3-[(hydroxyamino)carbonyl]-2-[(4-methoxyphenyl)sulfonyl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

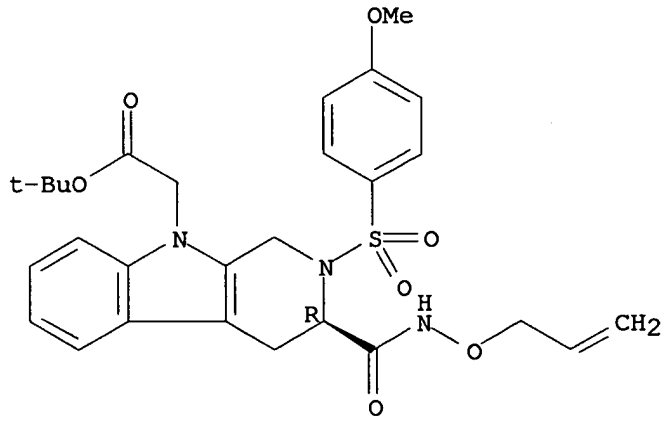


● HCl

IT **229974-84-9P 229974-85-0P 229974-86-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbolinecarboxamide derivs. as metalloprotease inhibitors)

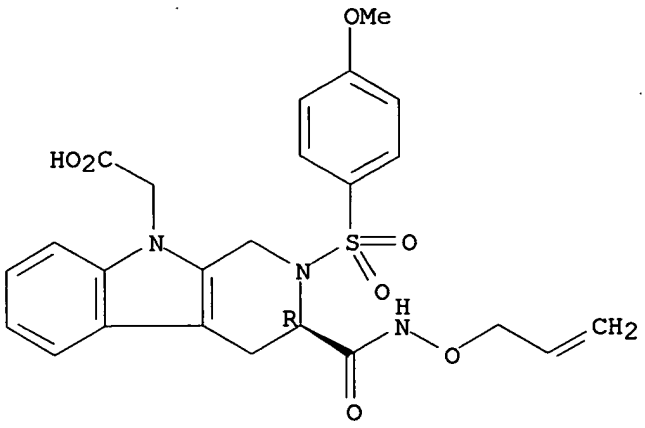
RN 229974-84-9 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-3-[[(2-propenyloxy)amino]carbonyl]-, 1,1-dimethylethyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



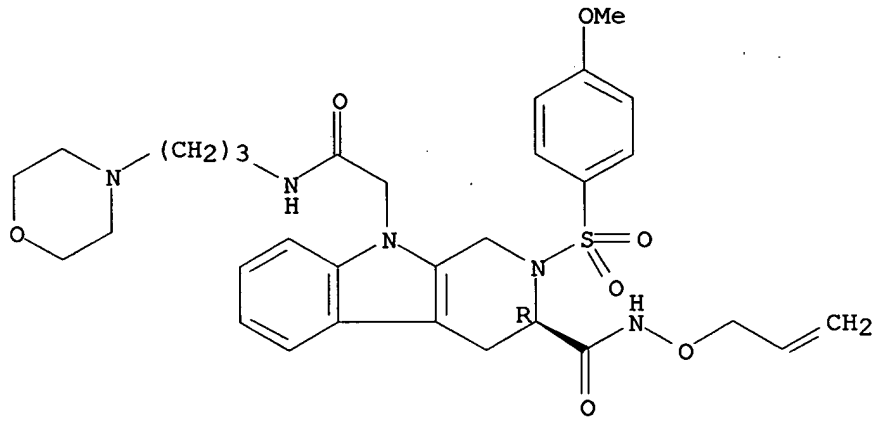
RN 229974-85-0 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetic acid, 1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-3-[[(2-propenyloxy)amino]carbonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 229974-86-1 CAPLUS
CN 9H-Pyrido[3,4-b]indole-9-acetamide, 1,2,3,4-tetrahydro-2-[(4-methoxyphenyl)sulfonyl]-N-[3-(4-morpholinyl)propyl]-3-[[(2-propenyloxy)amino]carbonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

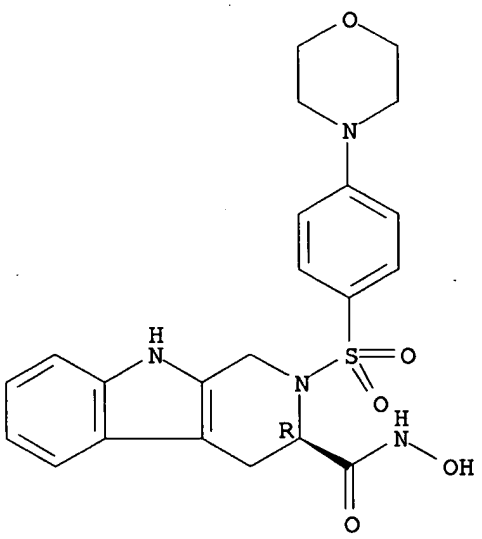
ACCESSION NUMBER:	1999:308109 CAPLUS
DOCUMENT NUMBER:	131:138914
TITLE:	Quantitative Structure-Activity Relationship of Human Neutrophil Collagenase (MMP-8) Inhibitors Using Comparative Molecular Field Analysis and X-ray Structure Analysis
AUTHOR(S):	Matter, Hans; Schwab, Wilfried; Barbier, Denis; Billen, Guenter; Haase, Burkhard; Neises, Bernhard; Schudok, Manfred; Thorwart, Werner; Schreuder, Herman; Brachvogel, Volker; Loenze, Petra; Weithmann, Klaus Ulrich
CORPORATE SOURCE:	Chemical Research Core Research Functions, Hoechst Marion Roussel, Frankfurt am Main, D-65926, Germany
SOURCE:	Journal of Medicinal Chemistry (1999), 42(11), 1908-1920 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB A set of 90 novel 2-(arylsulfonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylates and -hydroxamates as inhibitors of the matrix metalloproteinase human neutrophil collagenase (MMP-8) was designed, synthesized, and investigated by 3D-QSAR techniques (CoMFA, CoMSIA) and x-ray structure anal. Docking studies of a reference compound are based on crystal structures of MMP-8 complexed with peptidic inhibitors to propose a model of its bioactive conformation. This model was validated by a 1.7 Å x-ray structure of the catalytic domain of MMP-8. The 3D-QSAR models based on a superposition rule derived from these docking studies were validated using conventional and cross-validated r2 values using the leave-one-out method, repeated analyses using two randomly chosen cross-validation groups plus randomization of biol. activities. This led to consistent and highly predictive 3D-QSAR models with good correlation coeffs. for both CoMFA and CoMSIA, which were found to correspond to exptl. determined MMP-8 catalytic site topol. in terms of steric, electrostatic, and hydrophobic complementarity. Subsets selected as smaller training sets using 2D fingerprints and maximum dissimilarity methods resulted in 3D-QSAR models with remarkable correlation coeffs. and a high predictive power. This allowed to compensate the weaker zinc binding properties of carboxylates by introducing optimal fitting P1' residues. The final QSAR information agrees with all exptl. data for the binding topol. and thus provides clear guidelines and accurate activity predictions for novel MMP-8 inhibitors.

IT **191326-74-6 191326-90-6 191326-91-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(QSAR of (arylsulfonyl)tetrahydroisoquinoline carboxylates and -hydroxymates as human neutrophil collagenase (MMP-8) inhibitors)

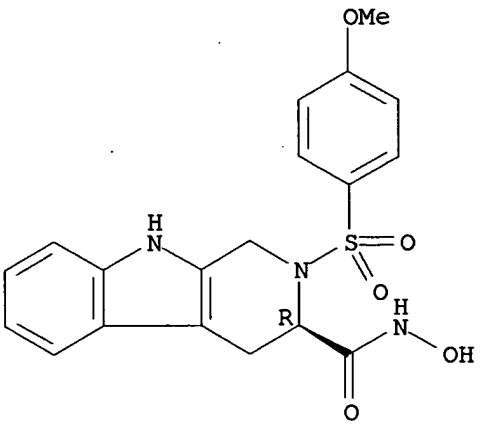
RN 191326-74-6 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[[4-(4-morpholinyl)phenyl]sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



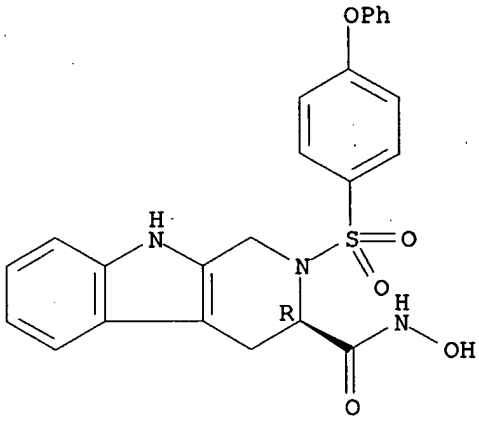
RN 191326-90-6 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 191326-91-7 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-phenoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:720114 CAPLUS
DOCUMENT NUMBER: 128:13253
TITLE: Fused pyridine N-hydroxy carboxamide derivatives and analogs as inhibitors of metalloproteases, process for their preparation, and pharmaceutical compositions containing them
INVENTOR(S): De Nanteuil, Guillaume; Paladino, Joseph; Remond, Georges; Atassi, Ghanem; Pierre, Alain; Tucker, Gordon; Bonnet, Jacqueline; Sabatini, Massimo
PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

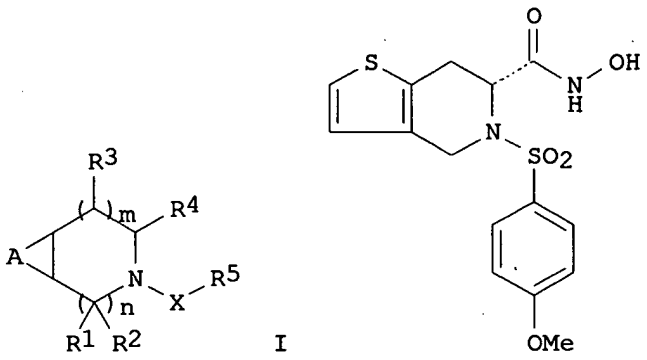
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 803505	A1	19971029	EP 1997-400913	19970423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
FR 2748026	A1	19971031	FR 1996-5321	19960426
FR 2748026	B1	19980605		
NO 9701862	A	19971027	NO 1997-1862	19970423
CA 2203618	AA	19971026	CA 1997-2203618	19970424
CA 2203618	C	20020528		
AU 9719121	A1	19971030	AU 1997-19121	19970424
AU 713680	B2	19991209		
ZA 9703647	A	19971119	ZA 1997-3647	19970425
CN 1165817	A	19971126	CN 1997-109728	19970425
JP 10059936	A2	19980303	JP 1997-108954	19970425
US 5866587	A	19990202	US 1997-842982	19970425

PRIORITY APPLN. INFO.: FR 1996-5321 A 19960426

OTHER SOURCE(S): CASREACT 128:13253; MARPAT 128:13253

GI



I II

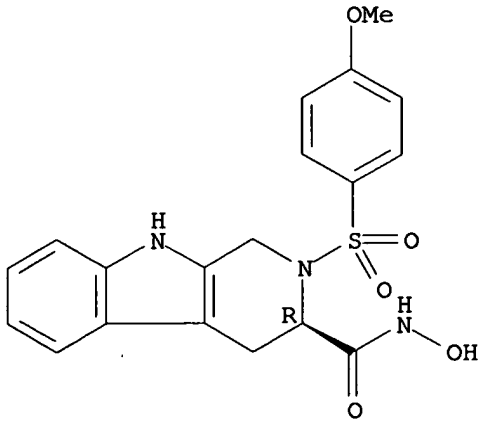
AB Title compds. I are disclosed [wherein m, n = 0, 1, 2; R1, R2 = H, alkyl, aralkyl, aryl; or R1R2 = O, alkylene; R3 = H, alkyl, OH, alkoxy, or aryl; R4 = CONR6OR6', CSNR6OR6', C(:NH)NR6OR6', CO2R7, NHCONHOH, NHCH2CO2R7, CH(NHR7')CO2R7, CH(CO2R7)2; X = SO2, CO, SO2NH; R5 = alkyl (optionally bearing halo, OH, alkoxy, aryl, or CO2R7), cycloalkyl, aryl, or heterocyclyl; R6, R6' = H or alkyl; R7, R7' = H, alkyl, aralkyl; A = fused aromatic (with provisos) or heterocyclic ring]. I are metalloprotease inhibitors, potentially useful for treatment of cancer, rheumatoid arthritis, atherosclerosis, etc. Examples include 30 syntheses of I, 19 prophetic compds., 4 biol. screens for selected compds., and a formulation. For instance, (R)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid hydrochloride underwent a sequence of N-sulfonylation with 4-MeOC6H4SO2Cl, amidation with H2NOCH2CH:CH2.HCl, and Pd-mediated deallylation, to give preferred title compound II. In tests for protection of guinea pig cartilaginous matrix against IL-1β-induced degradation, II gave 98% protection of collagens and 45% protection of proteoglycans.

IT **191326-90-6P 198957-28-7P 198957-29-8P**
198957-30-1P 198957-45-8P 198957-46-9P
198957-47-0P 198957-48-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridine N-hydroxy carboxamide derivs. and analogs as metalloprotease inhibitors)

RN 191326-90-6 CAPLUS

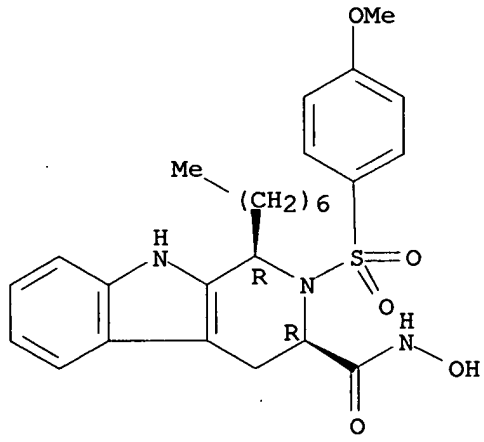
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



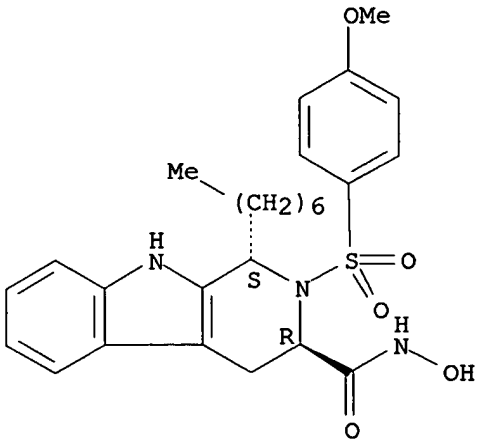
RN 198957-28-7 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 1-heptyl-2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (1R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



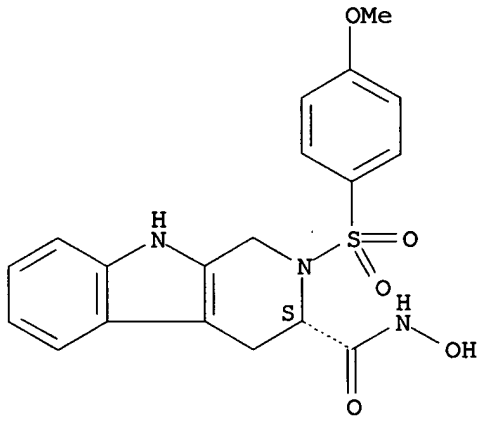
RN 198957-29-8 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 1-heptyl-2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



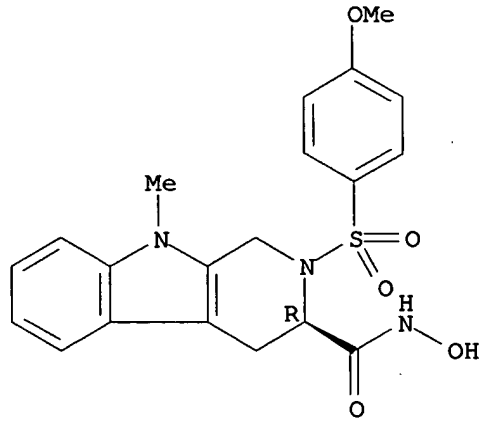
RN 198957-30-1 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



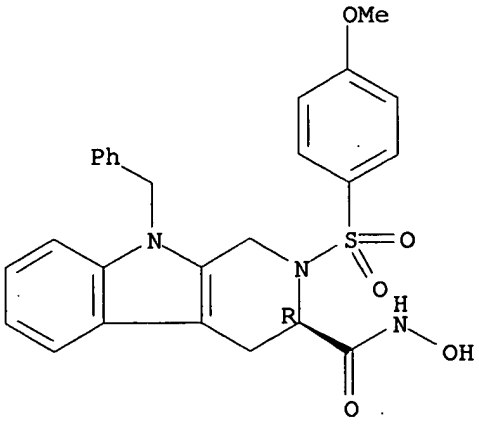
RN 198957-45-8 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-9-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



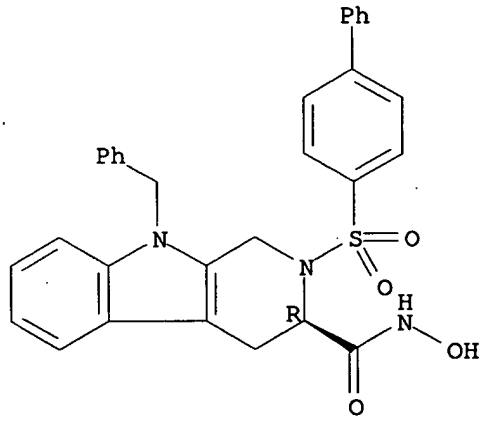
RN 198957-46-9 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-9-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



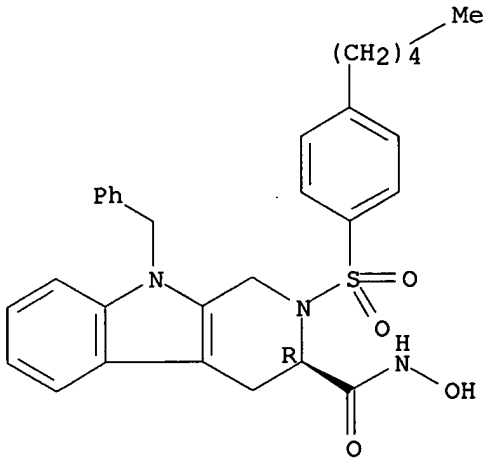
RN 198957-47-0 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2-([1,1'-biphenyl]-4-ylsulfonyl)-2,3,4,9-tetrahydro-N-hydroxy-9-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198957-48-1 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-pentylphenyl)sulfonyl]-9-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:443319 CAPLUS
DOCUMENT NUMBER: 127:65701
TITLE: Preparation of 2-arylsulfonylisoquinoline-3-carboxylic and hydroxamic acids and analogs as matrix metalloproteinase inhibitors
INVENTOR(S): Thorwart, Werner; Schwab, Wilfried; Schudok, Manfred; Haase, Burkhard; Bartnik, Eckart; Weithmann, Klaus-ulrich
PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9718194	A1	19970522	WO 1996-EP4776	19961104
W: AU, BG, BR, BY, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, RU, SG, SI, TR, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19542189	A1	19970515	DE 1995-19542189	19951113
DE 19612298	A1	19971002	DE 1996-19612298	19960328
AU 9675624	A1	19970605	AU 1996-75624	19961104
AU 707707	B2	19990715		
EP 861236	A1	19980902	EP 1996-938052	19961104
EP 861236	B1	20020213		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000500145	T2	20000111	JP 1997-518542	19961104
RU 2164914	C2	20010410	RU 1998-111153	19961104
AT 213232	E	20020215	AT 1996-938052	19961104
PL 186869	B1	20040331	PL 1996-326702	19961104
BR 9611479	A	19990713	BR 1996-11479	19970312
US 6207672	B1	20010327	US 1999-68497	19990309
US 2001011134	A1	20010802	US 2001-780514	20010212
US 6573277	B2	20030603		
US 2003176432	A1	20030918	US 2003-376287	20030303
US 6815440	B2	20041109		

PRIORITY APPLN. INFO.:			
DE 1995-19542189	A	19951113	
DE 1996-19612298	A	19960328	
WO 1996-EP4776	W	19961104	

US 1999-68497 A3 19990309
US 2001-780514 A3 20010212

OTHER SOURCE(S): MARPAT 127:65701

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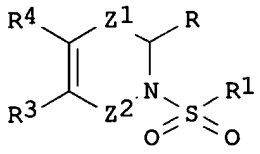
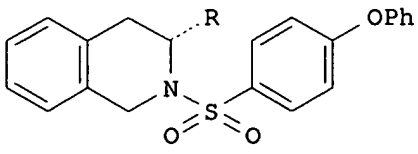


I



II

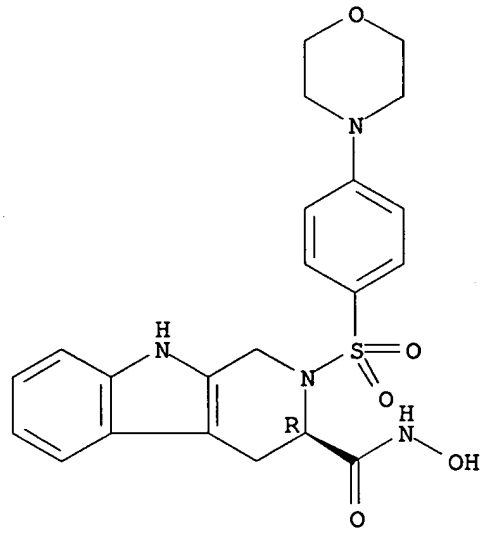
AB Title compds. [I; R = CO2H or CONHOH; R1 = (un)substituted phenyl(alkyl), -naphthyl, etc.; R3R4 = (un)substituted CH:CHCH:CH, atoms to complete a heterocyclic ring, etc.; Z1,Z2 = (CH2)0-2] were prepared Thus, Me (R)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate was N-sulfonate by 4-(PhO)C6H4SO2Cl and the product converted in 2 steps to title compound II (R = CONHOH). Data for biol. activity of I were given.

IT **191326-74-6P 191326-90-6P 191326-91-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-arylsulfonylisoquinoline-3-carboxylic and hydroxamic acids and analogs as matrix metalloproteinase inhibitors)

RN 191326-74-6 CAPLUS

CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[[4-(4-morpholinyl)phenyl]sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

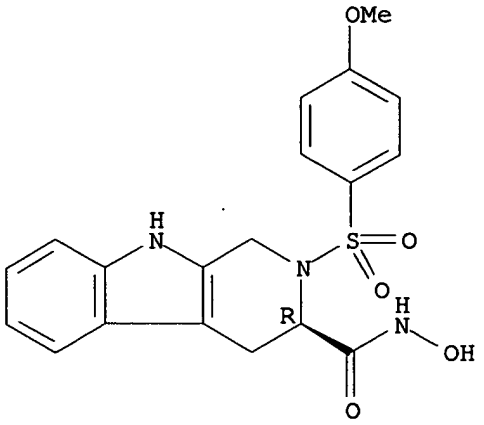
Absolute stereochemistry.



RN 191326-90-6 CAPLUS

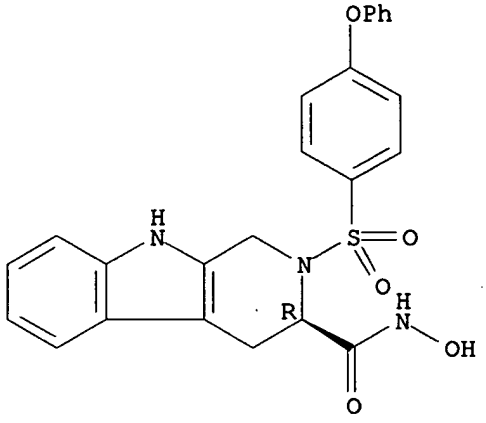
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-methoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 191326-91-7 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[(4-phenoxyphenyl)sulfonyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:244196 CAPLUS
DOCUMENT NUMBER: 126:220696
TITLE: Method for determining the therapeutic activity of metalloproteinase inhibitor compounds, new inhibitor compounds, and the therapeutic use thereof
INVENTOR(S): Politi, Vincenzo; D. Alessio, Silvana; Di Stazio, Giovanni; De Luca, Giovanna; Materazzi, Mario
PATENT ASSIGNEE(S): Polifarma S.P.A., Italy
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 758021	A2	19970212	EP 1996-830445	19960802
EP 758021	A3	19980722		
R: DE, ES, FR, GB				

US 5846755	A	19981208	US 1996-693021	19960806
JP 09136841	A2	19970527	JP 1996-208490	19960807
US 6057297	A	20000502	US 1998-40446	19980318
PRIORITY APPLN. INFO.:			IT 1995-RM557	A 19950807
			US 1996-693021	A3 19960806

OTHER SOURCE(S): MARPAT 126:220696

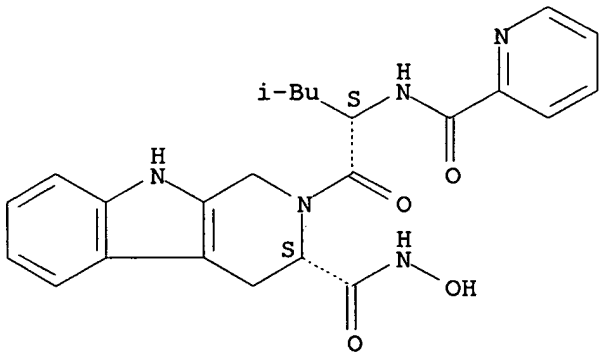
AB A method is disclosed for determining the activity as pharmacol. agents of zinc-dependent metalloproteinase-inhibiting peptidomimetic chemical compds. extracted from snake venom for the therapeutic treatment of disturbances created in mammals by metalloproteinases of endogenous origin. Also disclosed are inhibitor compds. determined in this way, as well as their pharmaceutical use in a variety of important human pathologies connected with endogenous metalloproteinase activation. Preparation of selected compds. of the invention is also described. The compds. may be used in the treatment of e.g. atherosclerosis or to e.g. influence immune response or antagonize the toxic effects of snake venom.

IT **187801-93-0P 187801-95-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(zinc-dependent metalloproteinase inhibitor compound identification method, peptidomimetic preparation, and therapeutic use)

RN 187801-93-0 CAPLUS

CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-2-[4-methyl-1-oxo-2-[(2-pyridinylcarbonyl)amino]pentyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

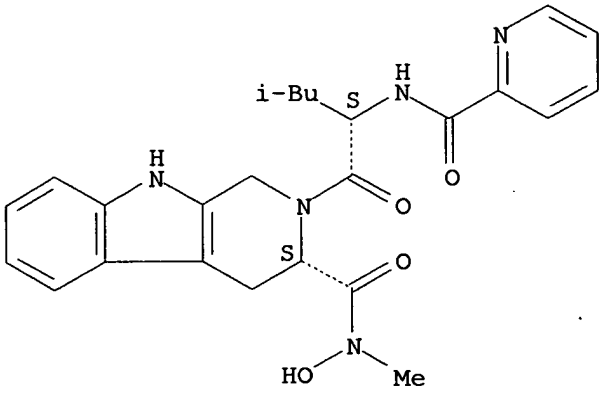
Absolute stereochemistry.



RN 187801-95-2 CAPLUS

CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-hydroxy-N-methyl-2-[4-methyl-1-oxo-2-[(2-pyridinylcarbonyl)amino]pentyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

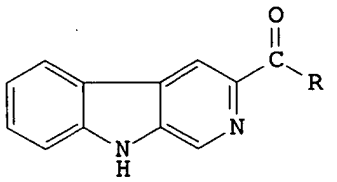
Absolute stereochemistry.



L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:632777 CAPLUS
DOCUMENT NUMBER: 111:232777
TITLE: New 3-substituted β-carbolines with benzodiazepine receptor-binding activity, processes and intermediates for their preparation, their use as medicaments, and pharmaceutical compositions containing them
INVENTOR(S): Gardner, Colin Robert; Hedgecock, Charles John Robert
PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.
SOURCE: Fr. Demande, 18 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2619817	A1	19890303	FR 1988-11243	19880826
FR 2619817	B1	19920117		
GB 2209032	A1	19890426	GB 1988-20218	19880825
GB 2209032	B2	19910731		

PRIORITY APPLN. INFO.: GB 1987-20125 A 19870826
OTHER SOURCE(S): MARPAT 111:232777
GI



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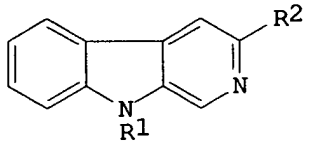


II

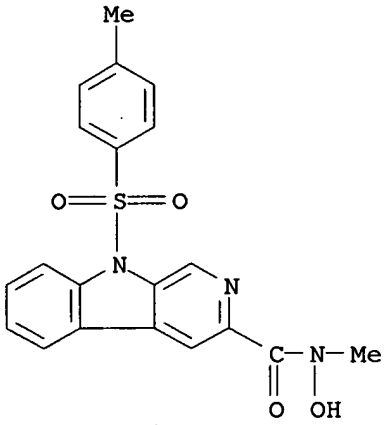
AB β-Carboline-derived ketones I (R = C3-6 cycloalkyl), which have a remarkable affinity for benzodiazepine receptors, were prepared from corresponding aldehydes II (R1 = protecting group; R2 = CHO). II (R1 = H, R2 = CHO) was silylated by NaH and Me3SiCl, then treated in situ with cyclopropylmagnesium bromide and worked up with NH4Cl to give II (R1 = H, R2 = cyclopropylhydroxymethyl). Oxidation of the alc. by MnO2 in CHCl3 gave I (R = cyclopropyl) (III). Tablets were prepared from 20 mg III and 150 mg excipient containing lactose, starch, talc, and Mg stearate. The IC50 of III

for inhibiting specific binding of [3H]-flunitrazepam (0.6 nmol) to benzodiazepine receptors in a rat brain membrane preparation was 0.7 nM.

IT **123819-70-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of benzodiazepine receptor-binding
β-carboline derivs.)

RN 123819-70-5 CAPLUS

CN 9H-Pyrido[3,4-b]indole-3-carboxamide, N-hydroxy-N-methyl-9-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



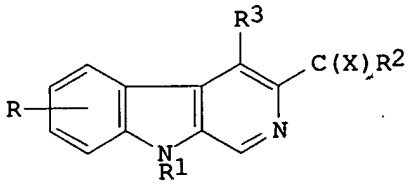
L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:515508 CAPLUS
DOCUMENT NUMBER: 95:115508
TITLE: Psychotropic β-carboline-3-carboxylates
PATENT ASSIGNEE(S): Schering A.-G., Fed. Rep. Ger.
SOURCE: Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 56043283	A2	19810421	JP 1980-119662	19800829
JP 02034952	B4	19900807		
DK 8000889	A	19810830	DK 1980-889	19800229
DE 3015816	A1	19811029	DE 1980-3015816	19800422
DE 3023567	A1	19820121	DE 1980-3023567	19800620
AU 8061864	A1	19810416	AU 1980-61864	19800819
AU 544731	B2	19850613		
EP 30254	A1	19810617	EP 1980-105019	19800823
EP 30254	B1	19841031		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 10098	E	19841115	AT 1980-105019	19800823
IL 60906	A1	19851129	IL 1980-60906	19800825
RO 80265	P	19830429	RO 1980-102050	19800827
FI 8002720	A	19810301	FI 1980-2720	19800828
FI 68829	B	19850731		
FI 68829	C	19851111		
NO 8002546	A	19810302	NO 1980-2546	19800828
NO 155055	B	19861027		

NO 155055	C	19870204				
US 4371536	A	19830201	US 1980-182244			19800828
CA 1150246	A1	19830719	CA 1980-359184			19800828
HU 28753	O	19831228	HU 1980-2129			19800828
HU 186744	B	19850930				
SU 1114335	A3	19840915	SU 1980-2969305			19800828
DK 8003703	A	19810301	DK 1980-3703			19800829
DK 168292	B1	19940307				
ES 494590	A1	19810816	ES 1980-494590			19800829
ZA 8005383	A	19810826	ZA 1980-5383			19800829
DD 152935	C	19811216	DD 1980-223673			19800829
US 5010077	A	19910423	US 1988-188145			19880425
PRIORITY APPLN. INFO.:			DK 1979-3622	A	19790829	
			DK 1980-889	A	19800229	
			DE 1980-3015816	A	19800422	
			DE 1980-3023567	A	19800620	
			DK 1979-6322	A	19790829	
			EP 1980-105019	A	19800823	
			US 1980-182244	A3	19800828	
			US 1982-433308	B1	19821007	
			US 1985-731244	B1	19850507	

OTHER SOURCE(S): CASREACT 95:115508

GI



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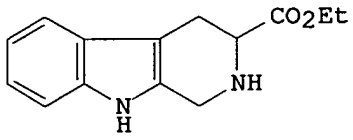


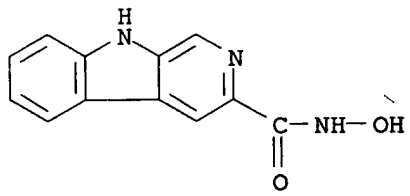
II

AB Psychotropics I (R = H, halo, amino, amido, NO2, cyano, carboxyl, alkoxycarbonyl, OH, alkoxy, SMe, sulfonamido; R1 = H, alkyl, alkoxycarbonyl; R2 = alkoxy, aryloxy,aralkoxy, amino; R3 = H, alkyl, cycloalkyl, aralkyl, Ph, alkoxyphenyl; X = S, O, NR4; R4 = H, alkyl, cycloalkyl) were prepared Thus, heating 15.0 g L-tryptophan with 6.07 mL 40% CH2O in 0.6 N NaOH at 53° 25 h followed by esterification gave 7.25 g II, which (7 g) was refluxed with 10 g chloranil in Cl2CHCHCl2 to give 1.5 g I (R = R1 = R3 = H, R2 = OEt, X = O) (III). III had an ED50 of 60 mg/kg s.c. in rats for inhibition of Flunitrazepam binding.

IT **78538-94-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 78538-94-0 CAPLUS

CN 9H-Pyrido[3,4-b]indole-3-carboxamide, N-hydroxy- (9CI) (CA INDEX NAME)



=> fil beilstein

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	61.08	222.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.76	-8.76

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FILE LAST UPDATED ON February 14, 2005

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*** FILE CONTAINS 9,133,317 SUBSTANCES ***

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.28	223.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.76

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L6 0 L3

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.43	224.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.76

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